UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,527	08/04/2006	Masaichi Hasegawa	TC00008	8681

20462 7590 02/06/2008

SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	**PAPER NUMBER**
4173	

NOTIFICATION DATE	DELIVERY MODE
02/06/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/588,527	HASEGAWA ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *3 and 4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,2 and 5-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 pages*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the following species: 2-(2-Amino-ethylamino)-6-quinolin-6-yl-3H-pyrimidin-4-one in the reply filed on December 21, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Examination was expanded to the following species: 2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone (example 44 on page 61 of the specification or the second compound from the bottom on page 83, claim 10).

Status of Claims

Claims 1-10 are currently pending and are the subject of this office action.

Claims 3-4 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 21, 2007.

Claims 1-2 and 5-10 are presently under examination.

Priority

The present application is a 371 of PCT/US05/02972 filed on 02/03/2005, and claims priority to provisional application No. 60/542,090 filed on 02/04/2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 5-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1 and 2 describe a compound of formula I (see claim 1), or a salt, solvate, or a physiologically functional derivative thereof. Claims 5-8 describe a method of inhibiting hYAK3 in a mammal (claim 5) or a method of treating or preventing diseases of the erythroid and hematopoietic systems (claims 6-8) comprising administering a compound of Formula I (see claim 5), or a salt, solvate, or a physiologically functional derivative thereof. Claim 9 describes a pharmaceutical composition including a therapeutically effective amount of a compound of formula I (see claim 9), or a salt, solvate, or a physiologically functional derivative thereof.

M.P.E.P. #2163 states: "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention....one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the

knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process".

While the specification describes compounds of general formula I (see claims 1 and 5) and more specifically: 2-(2-Amino-ethylamino)-6-quinolin-6-yl-3H-pyrimidin-4-one (species elected by applicant) and 2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone (extended species elected by examiner), it does not describe any solvate or physiologically functional derivative as to convey possession of the entire genus encompassed by solvate or physiologically functional derivative. The specification gives a definition of solvates (see page 13) and physiologically functional derivatives (see page 12), but does not specify a set of particular solvents or physiologically functional derivatives.

Given the broad scope of the claimed subject matter, Applicant has not provided sufficient written description that would allow the skilled artisan to recognize all the solvates or physiologically functional derivatives claimed.

Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without

undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996). As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1- the quantity of experimentation necessary,

2- the amount of direction or guidance provided,

3- the presence or absence of working examples,

4- the nature of the invention,

5- the state of the prior art,

6- the relative skill of those in the art,

7- the predictability of the art, and

8- the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping

that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention

Claims 6-8 describe a method of treating or preventing diseases of the erythroid and hematopoietic systems, caused by hYAK3 imbalance or inappropriate activity; comprising, administering to a mammal a therapeutically effective amount of a compound of formula I (see claim 6), or a salt, solvate, or a physiologically functional derivative thereof.

2. The state and predictability of the art

It is well established that "the scope of enablement varies with the degree of unpredictability of the factors involved" and physiological activity is considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved); *Nationwide Chemical Corporation, et. al. v. Wright, et. al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances); *Ex parte Sudilovsky* 21 USPQ2d 1702 (Applicant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable); *In re Wright* 27 USPQ2d 1510

(the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian vaccine was uncertain).

There is currently no prior art describing any treatment or prevention of diseases of the erythroid and hematopoietic systems by administering compounds that inhibit the activity of hYAK3.

3. The relative skill of those in the art

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

4. The breadth of the claims

Claims 6-8 recite a very broad genus of diseases to be treated with a very broad genus of compounds.

5. The amount of direction or guidance provided and the presence or absence of working examples

The specification fails to disclose any data to support the fact that any of the compounds of Formula I could prevent or treat any disease of the erythroid and hematopoietic systems. The specification only provides an *in vitro* hYAK3 kinase assay. There is no cellular or *in vivo* data to corroborate that these compounds could prevent or treat any disease of the erythroid and hematopoietic systems. The rationale

that applicant uses to reach these conclusions is that the presence of YAK3 proteins in hematopoietic tissues, and that the RNA is expressed at significant levels in erythroid or erythropoietin responsive cells. All these arguments suggest that YAK3 might play a role in the diseases of the erythroid and hematopoietic systems, and definitively is an invitation for further research in the area. However, these arguments and the data provided do not demonstrate at all that inhibitors of YAK3 could treat any of these diseases.

6. The quantity of experimentation necessary

In the absence of previous examples in the prior art, and in the absence of experimental evidence commensurate with the scope of the claims, how is the skilled physician supposed to know how to treat, for example, a subject with anemia? Which of the many compounds encompassed by formula I is he supposed to choose among? Which of these compounds will show any real efficacy in a human? Which doses, formulation and or /routes of administration is he supposed to use? This would require to run in vivo animal data for several compounds, optimize the best compounds, run pre-clinical and clinical trials or testing in an assay known to correlate to clinical efficacy of such treatment. This is undue experimentation given the limited guidance and direction provided by Applicants.

Accordingly, the inventions of claims 6-8 do not comply with the enablement requirement of 35 U.S.C 112, first paragraph, since to practice the claimed invention a

person of ordinary skill in the art would have to engage in undue experimentation with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 9 and 10 rejected under 35 U.S.C. 102(b) as being anticipated by Watanabe et. al. (WO2000/18758 cited by applicant).

Claim 5 recites a method of inhibiting hYAK3 in a mammal; comprising, administering to the mammal a therapeutically effective amount of a compound of formula I (for example 2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone), or a salt, solvate, or a physiologically functional derivative thereof.

Watanabe et. al. teach the administration of pyrimidone derivatives of Formula I (see abstract) (2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone in particular, see page 25, table 1, example 54; or page 73, example 20 for preparation of this compound) for the treatment of Alzheimer disease in humans (see abstract). Watanabe et. al. are silent regarding inhibiting hYAK3 in a mammal. However, inhibition of hYAK3 is an inherent property of this compound (i.e. it was already present in the prior art, even though the prior art does not recognize that property). In this

regard applicant refers to MPEP 2112, section I entitled: "Something which is old does not become patentable upon the discovery of a new property". It further states: "The discovery of a previously unappreciated property of a prior art composition for the prior art's functioning, does not render the old composition patentably new to the discoverer". *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property, which is inherently present in the prior art, does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that: just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel". By practicing the invention of Watanabe et. al.: "administering 2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone to patients with Alzheimer disease", one would be practicing the invention of claim 5: "inhibiting hYAK3 in a mammal with 2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone".

Claim 9 recites a pharmaceutical composition including a therapeutically effective amount of a compound of Formula I (2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone in particular), and one or more pharmaceutically active carriers, diluents and excipients.

For claim 9, Watanabe et. al. teach a pharmaceutical composition of pyrimidone derivatives of Formula I (see abstract) (2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone in particular, see page 25, table 1, example 54; or page 73, example 20 for preparation of this compound) , which comprises also one or more pharmaceutical additives (see page 66, lines 4-end and page 67 lines 1-until end of second paragraph).

Claim 10 recites: a compound selected from the group consisting of:

2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone (see second compound from the bottom on page 83, claim 10).

Watanabe et. al. teach the compound 2-{[3-(methyloxy)phenyl]amino}-6-(4-pyridinyl)-4(1H)-pyrimidinone (see page 25, table 1, example 54; or page 73, example 20 for preparation of this compound).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward can be reached on 571 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MLS
January 24, 2008

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600